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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,719	11/26/2003	Thomas Herget	AXM-009.3 US	4255

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,719	HERGET ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/13/2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-10,12-14 and 36-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-10,12-14 and 36-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/27/2006*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *1/30/2007*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

This is a response to the amendment filed on 11/28/06. Claims 4-10 and 12-14 have been amended. Claims 1-3, 11 and 15-35 have been canceled. New claims 36-39 have been added. Claims 4-10, 12-14 and 36-39 are pending and considered before the examiner.

Priority

1. Applicant is still reminded that benefit of the effective filing date of the amended claims is still based on filing date of the parent Application No. 10,342,054 on Jan. 14, 2003.

2. To obtain the foreign priority under 35 C.F. 35 U.S.C. 119(a)-(d) or (f), applicants still required to satisfy the requirement of 37 CFR 1.55(a)(2) of providing a certified copy of the foreign application. Applicant may simply identify the application containing the certified copy.

Claim Rejections - 35 USC § 112

3. The rejection of claims 4-14 under 35 U.S.C. 112, second paragraph has been withdrawn necessitated by applicants' amendment.

4. The rejection of claims 4-8, 10-14 under 35 U.S.C. 112, first paragraph has been removed necessitated by applicants' amendment.

Claim Rejections - 35 USC § 102

5. Applicant's arguments with respect to rejection of claims 4-14 under 35 U.S.C. 102(b) as being anticipated by Look et al. (Antiviral Research 1999, Vol. 43, pp. 113-122) have been considered and the rejection has been withdrawn.

6. Applicant's arguments with respect to rejection of claims 9 and 11 under 35 U.S.C. 102(b) as being anticipated by Rumin et al, (WO 99/67362A1) have been considered and withdrawn.

7. However, a new ground(s) of rejection for the claims are established necessitated by applicants' IDS provided on July 27, 2006 after applicants reviewed the first office action mailed on May 04, 2006.

New Ground rejections:

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by Chu et al. (J. of Nutrition, 1999, Vol. 129, pp. 1846-1854).

9. Chu et al. teach a method of induction of a Gpx2 gene expression in mammalian cell lines including the epithelial cells of gastrointestinal (GI) tract by incubating the cells in the presence of selenium salt and retinoid acid (RA), wherein the gene Gpx2 encodes the gastrointestinal (GI) glutathione peroxidase (GPX-GI). They point out that said enzyme is previously proved to be the selenium-dependent glutathione peroxidase, and they further found that Gpx2 gene is also up-regulated by retinoid acid (AR) in the presence of selenium slat (See Abstract, methods on page 1847, Table 2, Figs 5-6). Therefore, claim 9 is anticipated by the cited reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

10. (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Esworthy et al. (Biochemical et Biophysica Acta. 1998, Vol. 1381, pp. 213-226) and Chu et al. (J. Nutrition 1999, Vol. 129, pp. 1846-1854).

12. Claim 8 is directed to induction the expression and activity of human cellular protein gastrointestinal glutathione peroxidase (GPX-GI) in an individual by selenium or selenium salt and retinoid or retinoic acid in combination.

13. Esworthy et al. teach that human cellular protein gastrointestinal glutathione peroxidase (GPX-GI) or its mRNA of said gene Gpx2 gene are induced and up-regulated by selenium

compound in a dose dependent manner after they administrate the selenium compound into a rat (See Figs. 1-7). Esworthy et al. do not teach that retinoid compound can induce the GPX-GI and its gene expression or activity in vitro and/or in vivo

14. Chu et al. teach that the selenium-dependent gastrointestinal glutathione peroxidase GPX-GI encoded by the Gpx2 gene is highly expressed in the epithelium of the gastrointestinal (GI) tract and sporadically in breast tissue, wherein said GPX-GI protein level and its gene Gpx2 expression can also be up-regulated by retinoid acid in the presence of selenium salt. They concluded that such up-regulation of GPX-GI protein level and its gene Gpx2 by retinoic acid has an important function of protecting epithelial cell from damage caused by active oxidative stress.

15. Therefore, it would have been obvious for a person having ordinary skill in the art at the time to be motivated by combining the teachings from Esworthy et al. and Chu et al. in order to further promote the expressions of GPX-GI protein and its gene Gpx2 gene for protecting the oxidative stress in an epithelium. Because selenium and retinoid are both proved to be positive regulatory agents for GPX-GI protein and its gene Gpx2.

16. Hence, the claimed invention as a whole is prima facie obvious absence unexpected results.

Claim Rejections - 35 USC § 103

17. Claims 4-7, 10, 12-14 and 36-39 are rejected under 35 U.S.C. 103(a) as obvious over Hellstrand et al. (US patent 6,242,473B1) and Albrecht et al. (US Patent 6,172,046B1) in view of Chu et al. (J. Nutrition 1999, Vol. 129, pp. 1846-1854) and Esworthy et al. (Biochemical et Biophysica Acta. 1998, Vol. 1381, pp. 213-226) in light of Reddy et al. Hapatology Feb. 2001, pp. 433-438.

18. The claims 4-7, 10, 12-14 and 36-39 are directed to a method for treating HCV infection and **its associated disease** by administration of selenium or selenium salt in combination a retinoic or retinoic acid salt to the cell culture or to an individual, wherein the method further comprises administering anti-HCV agent including interferon-α (INF-α), preferably peglyated INF-α in combinantion with ribavirin.

19. Hellstrand et al. teach a method for treating the disease cause by HCV infection that is related to the cell damages. The method comprises treating the individual with effective amounts of compounds including a reactive oxygen metabolites (ROM) scavenger and a ROM production and release inhibiting compound in addition to an anti-HCV treatment, wherein the ROM scavenger compounds include glutathione peroxidase and ROM production and release inhibiting compounds include retinoid compound, The anti-HCV agent is alpha-interferon (α-INF) (See columns 15-16 and claims 1-12). Hellstrand et al. also teach that Minerals such as selenium can also be efficacious in combating ROM-mediated damage (See lines 30-59 on column 4). Hellstrand et al. teach that mechanism of using such compounds including glutathione peroxidase can combat the cell damage caused by HCV infection via reducing the active oxidative stress in the cells upon the virus infection.

20. Hellstrand et al. do not particularly teach using the combination of selenium and retinoid for stimulating the GPX-IG production and its activity, and using pegylated α-INF optionally with ribavirin together for treating HCV infection associated disease.

21. Esworthy et al. teach that human cellular protein gastrointestinal glutathione peroxidase (GPX-GI) or its mRNA of said gene Gpx2 gene are induced by selenium compound in a dose dependent manner after they administrate the selenium compound into a rat, the selenium compound induces GPX-GI activity and expression of Gpx2 from the mucosal epithelial cells in the animal GI tract (See Figs. 1-7).

22. Chu et al. teach that the selenium-dependent gastrointestinal glutathione peroxidase GPX-GI encoded by the Gpx2 gene is highly expressed in the epithelium of the gastrointestinal (GI) tract and sporadically in breast tissue, wherein said GPX-GI protein level and its gene Gpx2 expression are also up-regulated by retinoid acid in the presence of selenium salt. They concluded that such up-regulation of GPX-GI protein level of gene Gpx2 in an epithelium-specific manner by retinoic acid have an important function for protecting epithelial cell from the active oxidative stress (See Figs. 1-7 and last paragraph in page 1853).

23. Albrecht et al. teach that a combination therapy of HCV infection using a therapeutic effective amount ribavirin and a therapeutic effective amount of α-INF especially including the pegylated α-INF (Claims 1-10) are very effective, wherein said method can reach to the level of

eradicating detectable HCV-RNA in patients having chronic HCV infection. While Albrecht et al. do not explicitly teach the advantage of utilizing pegylated α-INF, it is well known for any ordinary skill in the art that pegylated α-INF has an advantages of releasing an effective amount of α-INF in the blood stream slowly and gradually, protecting it from a quick degradation in the blood stream as well as reducing the side effect caused by the large amount of α-INF in the blood stream (Please see the article by Reddy et al. Hepatology Feb. 2001, pp. 433-438).

24. Therefore, it would have been obvious for a person having ordinary skill in the art at the time of the invention was filled to be motivated by combining the method taught by Hellstrand et al. in view of Chu et al. Esworthy et al. and further adapting the method by Albrecht et al. in light of Reddy et al. to get an improved therapeutic effect against disease caused by HCV infection. Because the art prior to the application was filed had already taught that the selenium, glutathione peroxide and retinoid compound can be used for treating the disease caused by HIV infection, and up-regulation of glutathione peroxidase in the GI tract can be achieved by selenium and retinoid acid compound used together. Moreover, the advantage of using peglyated INF and rebavirin in combination are well recognized in the art than using non-protected INF alone. The combination of selenium and retinoic acid plus pegylated α-INF and ribavirin would be certainly more effective for combating the cell damage caused by HCV infection. The examine emphasizes that the method is also directed to the treatment of HIV associated disease.

25. Hence, the claimed invention as a whole is prima facie obvious absence unexpected results.

Conclusion

No claims are allowed.

26. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

27. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on July 27, 2006 also prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See

MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

28. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

31. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bao Qun Li
2/1/2007

JON WEBER
SUPERVISORY PATENT EXAMINER